Art Unit: 1645

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

We Claim:

1. (Withdrawn): A method of enhancing an immune response to an antigen in a mammal, comprising administering to the mammal a safe and effective amount of 1) an IL-18 polypeptide or bioactive fragment or variant thereof, and 2) an immunogenic composition comprising an antigen or immunogenic derivative thereof and a CpG adjuvant.

- 2. (Withdrawn): The method according to claim 2, wherein the antigen or immunogenic derivative thereof is derived from an organism selected from the group of: Human Immunodeficiency virus HIV-1, human herpes simplex viruses, cytomegalovirus, Rotavirus, Epstein Barr virus, Varicella Zoster Virus, from a hepatitis virus such as hepatitis B virus, hepatitis A virus, hepatitis C virus and hepatitis E virus, from Respiratory Syncytial virus, parainfluenza virus, measles virus, mumps virus, human papilloma viruses, flaviviruses or Influenza virus, from Neisseria spp, Moraxella spp, Bordetella spp; Mycobacterium spp., including M. tuberculosis; Escherichia spp, including enterotoxic E. coli; Salmonella spp.; Listeria spp; Helicobacter spp; Staphylococcus spp., including S. aureus, S. epidermidis;; Borrelia spp; Chlamydia spp., including C. trachomatis, C. pneumoniae; Plasmodium spp., including P. falciparum; Toxoplasma spp., and Candida spp.
- 3. (Withdrawn): A method of reducing the severity of a cancer in a patient, comprising administering to a patient in need thereof a safe and effective amount of 1) an IL-18 polypeptide or bioactive fragment or variant thereof and 2) an immunogenic composition comprising a tumour-associated antigen or immunogenic derivative thereof and a CpG adjuvant.
- 4. (Withdrawn): The method according to claim 3, wherein the tumour-associated antigen or immunogenic derivative thereof is selected from the group of: an antigen from the MAGE family, PRAME, BAGE, LAGE 1, LAGE 2, SAGE, HAGE, XAGE, PSA, PAP, PSCA, prostein, P501S, HASH2, Cripto, B726, NY-BR1.1, P510, MUC-1, Prostase, STEAP, tyrosinase, telomerase, survivin, CASB616, P53, and her 2 neu.
- 5. (Withdrawn): The method according to claim 1, wherein the IL-18 polypeptide or bioactive fragment or variant thereof and the immunogenic composition are administered simultaneously, separately or sequentially in any order.

Art Unit: 1645

6. (Withdrawn): The method according to claim 5, wherein the IL-18 polypeptide or bioactive fragment or variant thereof and the immunogenic composition are administered simultaneously in the form of a combined pharmaceutical preparation.

- 7. (Withdrawn): The method according to claim 1, wherein the IL-18 polypeptide or bioactive fragment or derivative thereof is from human or murine origin.
- 8. (Withdrawn): The method according to claim 7, wherein IL-18 is the polypeptide of SEQ ID NO.6 or SEQ ID NO.7 or bioactive fragment or derivative thereof.
- 9. (Withdrawn): The method according to claim 1, wherein the CpG adjuvant comprises a Purine, Purine, C, G, pyrimidine, pyrimidine sequence.
- 10. (Withdrawn): The method according to claim 1, wherein said CpG adjuvant is selected from the group of: TCC ATG ACG TTC CTG ACG TT (SEQ ID NO:1); TCT CCC AGC GTG CGC CAT (SEQ ID NO:2); ACC GAT GAC GTC GCC GGT GAC GGC ACC ACG (SEQ ID NO:3); TCG TCG TTT TGT CGT TTT GTC GTT (SEQ ID NO:4); and TCC ATG ACG TTC CTG ATG CT (SEQ ID NO:5).
- 11. (Withdrawn): The method according to claim 1, wherein said CpG adjuvant contains at least two unmethylated CG repeats that are separated at least by 3 nucleotides.
- 12. (Withdrawn): The method according to claim 11, wherein the immunostimulatory oligonucleotide contains at least two unmethylated CG repeats that are separated by 6 nucleotides.
- 13. (Previously presented): A combined preparation comprising as active ingredients the following individual components: (1) an IL-18 polypeptide or bioactive fragment or variant thereof and (2) immunogenic composition comprising an antigen and a CpG adjuvant, the active ingredients being for the simultaneous, separate or sequential use for the prophylaxis and/or treatment of infectious diseases, cancer, autoimmune diseases and related conditions.
- 14. (Previously presented): The combined preparation according to claim 13, wherein components (1) and (2) are admixed in a composition.
- 15. (Previously presented): The combined preparation according to claim 13, wherein the immunogenic composition comprises a tumour-associated antigen or immunogenic derivative thereof and is prophylactically or therapeutically active against cancer.

Art Unit: 1645

16. (Previously presented): The combined preparation according to claim 15, wherein the tumour-associated antigen or immunogenic derivative thereof is selected from the group of: an antigen from the MAGE family, PRAME, BAGE, LAGE 1, LAGE 2, SAGE, HAGE, XAGE, PSA, PAP, PSCA, prostein, P501S, HASH2, Cripto, B726, NY-BR1.1, P510, MUC-1, Prostase, STEAP, tyrosinase, telomerase, survivin, CASB616, P53, and her 2 neu.

- 17. (Previously presented): The combined preparation according to claim 13, wherein the IL-18 polypeptide or bioactive fragment or derivative thereof is from human or murine origin.
- 18. (Currently amended): The combined preparation according to claim 17, wherein IL-18 is the polypeptide of SEQ ID NO:[.]6 or SEQ ID NO:[.]7, or an a bioactive fragment or derivative thereof.
- 19. (Currently amended): The combined preparation according to claim 13, wherein the CpG adjuvant comprises a Purine, [Purine,] C, G, pyrimidine, pyrimidine sequence.
- 20. (Currently amended): The combined preparation as claimed in claim 13, wherein the immunogenic composition additionally comprises an immunostimulant chemical selected from the group of: 3D-MPL, QS21, a mixture of QS21 and cholesterol, aluminium hydroxide, aluminium phosphate, tocopherol, and an <u>oil-in-water</u> [oil in water] emulsion.
- 21. (Currently amended): The combined preparation as claimed in claim 20, wherein the immunogenic composition adjuvant comprises 3D-MPL, CpG, QS21, cholesterol, and an oil-in-water [oil in water] emulsion.
- 22. (Currently amended): The combined preparation as claimed in claim 21, wherein the <u>oil-in-water</u> [oil in water] emulsion comprises squalene, tocopherol, and polyoxyethylenesorbitan monooleate (Tween 80).
- 23. (Currently amended): The combined preparation as claimed in claim 20, wherein the immunogenic composition comprises QS21, cholesterol, and a CpG adjuvant.
- 24. (Previously presented): The combined preparation as claimed in claim 13, wherein both active components are in the form of injectable solutions.

Art Unit: 1645

25. (Currently amended): A pharmaceutical kit comprising as active ingredients the following individual components: (1) an IL-18 polypeptide or bioactive fragment thereof; and (2) an immunogenic composition comprising an antigen or immunogenic derivative thereof and a CpG adjuvant, the active ingredients being for the simultaneous, separate or sequential use for the prophylaxis and/or treatment of <u>a disease chosen from the group of: an infectious disease[s], a cancer, and an auto-immune disease[s].</u>

- 26. (Previously presented): The pharmaceutical kit according to claim 25, wherein the immunogenic composition comprises a tumour-associated antigen or immunogenic derivative thereof and is prophylactically or therapeutically active against cancer.
- 27. (Previously presented): The pharmaceutical kit according to claim 26, wherein the tumour-associated antigen or immunogenic derivative thereof is selected from the group of: an antigen from the MAGE family, PRAME, BAGE, LAGE 1, LAGE 2, SAGE, HAGE, XAGE, PSA, PAP, PSCA, prostein, P501S, HASH2, Cripto, B726, NY-BR1.1, P510, MUC-1, Prostase, STEAP, tyrosinase, telomerase, survivin, CASB616, P53, and her 2 neu.
 - 28. (Withdrawn): The combined preparation as claimed in claim 13 for use in medicine.
- 29. (Withdrawn): The method as claimed in claim 1 that comprises the use of a combined preparation comprising as active ingredients the following individual components: (1) an IL-18 polypeptide or bioactive fragment or variant thereof and (2) immunogenic composition comprising an antigen and a CpG adjuvant, the active ingredients being for the simultaneous, separate or sequential use for the prophylaxis and/or treatment of infectious diseases, cancer, autoimmune diseases and related conditions.

30.-35. (Cancelled)

- 36. (Withdrawn): A method of treating a patient suffering from or susceptible to infectious diseases, cancer, autoimmune diseases and related conditions comprising administering an IL-18 polypeptide or bioactive fragment or derivative thereof to the patient, wherein the patient has already been primed with an immunogenic composition comprising an antigen or immunogenic derivative thereof and a CpG adjuvant.
- 37. (Withdrawn): A method of treating a patient suffering from or susceptible to infectious diseases, cancer, autoimmune diseases and related conditions comprising administering an immunogenic composition comprising an antigen or immunogenic derivative thereof and a CpG

Art Unit: 1645

adjuvant to the patient, wherein the patient has already been primed with an IL-18 polypeptide or bioactive fragment or derivative thereof.

- 38. (Withdrawn): The method as claimed in claim 36, wherein the antigen is a tumour-associated antigen, and the cancer is selected from the group of: breast cancer, lung cancer, NSCLC, colon cancer, melanoma, ovarian cancer, bladder cancer, head and neck squanmous carcinoma, and esophageal cancer.
- 39. (Withdrawn): The method according to claim 36, wherein the IL-18 polypeptide or bioactive fragment or derivative thereof is from human or murine origin.
- 40. (Withdrawn): The method according to claim 39, wherein IL-18 is the polypeptide of SEQ ID NO:6 or SEQ ID NO:7 or bioactive fragment or derivative thereof.
- 41. (Currently amended): The method according to claim 26, wherein the CpG adjuvant comprises a Purine, [Purine,] C, G, pyrimidine, pyrimidine sequence.
- 42. (Currently amended): The combined preparation as claimed in claim 13, wherein the immunogenic composition additionally comprises at least two immunostimulant chemicals selected from the group of: 3D-MPL, QS21, a mixture of QS21 and cholesterol, aluminium hydroxide, aluminium phosphate, tocopherol, and an oil-in-emulsion [oil in water] emulsion.